

R E M A R K S

The Examiner is respectfully requested to acknowledge receipt of the certified copies of the priority documents that were filed on August 20, 2001.

The September 26, 2003 Office Action enclosed copies of the INFORMATION DISCLOSURE STATEMENT BY APPLICANT Form PTO/SB/08A dated December 3, 2002 and the Forms PTO/SB/08A and PTO/SB/08B dated June 20, 2003, with the Examiner's initials in the left column next to each cited publication.

Next to the citations of JP 59-210871 and JP 60-094075 at the bottom of the copy of the December 3, 2002 Form PTO/SB/08A that was returned with the Office Action, the Examiner made a handwritten notation of "ABS only". It is considered that "ABS" means "Abstract". It is respectfully submitted that no notation should have been placed next to the initialed publications on the aforesaid copy of the December 3, 2002 Form PTO/SB/08A, based on the following statement on page 600-132 (in Section 609) of the MPEP:

"The examiner should not require that a translation be filed by applicant. The examiner should not make any comment such as that the non-English language information has only been considered to the extent understood, since this fact is inherent."

JP 59-210871 and JP 60-094075 were cited in the European Search Report of the corresponding European application. This satisfies the statement of relevance required by the Patent Office Rules. See page 630-122 in Section 609 of the MPEP which states as follows:

"Where the information listed is not in the English language, but was cited in a search report or other action by a foreign patent office in a counterpart foreign application, the requirement for a concise explanation of relevance can be satisfied by submitting an English-language version of the search report or action which indicates the degree of relevance found by the foreign office. This may be an explanation of which portion of the reference is particularly relevant, to which claims it applies, or merely an 'X', 'Y', or 'A' indications on a search report."

In view of the above, it is respectfully submitted that the Examiner's notation of "ABS" next to these two publications is not appropriate.

Applicants have provided the following comments concerning JP 59-210871 and JP 60-094075. Applicants fully reviewed the two Japanese-language publications and found that there is no mention of anserine, dipeptides, D-ribose or any of the related substances for anti-fatigue composition in these publications.

Instead, the publications deal only with selected amino acids, histidine, lysine, arginine, leucine, isoleucine and valine in combination with vitamin E and either sodium ions or calcium ions.

The Examiner is therefore respectfully requested to return another initialed copy of said Form PTO/SB/08A dated December 3, 2002, without any notations thereon.

The Examiner is also respectfully requested to return a copy of the Form PTO/SB/08A dated July 15, 2004 with the Examiner's initials in the left column next to the cited publication.

Claim 1 was amended to include the feature of claim 20.

Claim 7 was amended to include the feature of claim 21.

The term "synergistic" recited in amended claims 1 and 7 is supported in the specification on page 7, line 4.

Claims 6 and 12 were amended into independent format. Claim 6 was amended to include the features of claim 1. Claim 12 was amended to include the features of claim 7.

New claims 22 to 25 and 27 to 31 are supported in the specification on page 7 lines 18 to 21.

New claims 26 and 31 are supported in the specification on page 7, lines 14 to 17.

Claim 21 was rejected under 35 USC 112, second paragraph, for the reason set forth at the middle of page 2 of the May 4, 2004 Office Action.

This rejection is avoided by the above amendments.

It is respectfully submitted that the present claims comply with all the requirements of 35 USC 112.

Applicants are pleased to note that claim 21 was deemed to be allowable at the middle of page 7 of the Office Action. Since the feature of claim 21 has been included in claims 1 and 7, it is respectfully submitted that all the present claims should be allowable.

Claims 1, 3, 5 and 20 were rejected under 35 USC 103 as being unpatentable over JP 61-181357 for the reasons set forth at the top of page 3 of the May 4, 2004 Office Action.

It was admitted in the May 4, 2004 Office Action that JP 61-181357 lacks the specific combination of anserine and ribose.

JP 61-181357 concerns a beef flavor composition containing a dipeptide which can be carnosine, balenine or anserine, and a sugar which could be glucose or ribose. The flavored composition can be made from a solution containing 100 parts of one or more dipeptides

such as carnosine, balenine or anserine with 10 to 400 parts of a sugar such a glucose or ribose, in water.

Claims 1, 3, 5 to 7, 9 and 11 to 16 were rejected under 35 USC 103 as being unpatentable over Hageman et al. USP 6,420,342 in view of Harris et al. USP 5,965,596 for the reasons set forth at the bottom of page 3 and continuing to the bottom of page 4 of the May 4, 2004 Office Action.

It was admitted in the May 4, 2004 Office Action that anserine is not specified in Hageman et al.

Claims 1, 3, 5 to 7, 9 and 11 to 16 were rejected under 35 USC 103 as being unpatentable over Harris et al. USP 5,965,596 in view of St. Cyr et al. USP 6,159,942 for the reasons set forth on page 5 of the May 4, 2004 Office Action.

It was admitted in the May 4, 2004 Office Action that Harris et al. do not teach the inclusion of ribose.

Hageman et al. disclose a nutritional composition which is stated to be useful for the prevention or treatment of various diseases. The Hageman et al. composition comprises ribose and folate as essential components. In column 13, lines 20 to 35 of Hageman et al., a composition containing ribose, folic acid and yeast extract is disclosed.

The several conditions and diseases described in column 5, lines 39 to 52 of Hageman et al. (such as trauma; surgery; inflammation; subfertility; laceration problems; gut disorders; jaundice; cancer; arthritis; vascular problems; ischaemia; aging; respiratory infections; impaired immune function; burns; sepsis; malnutrition; malaria; cystic fibrosis; migraine; neurological problems including Huntington's disease, Parkinson's disease, Alzheimer's disease, schizophrenia and depression; and pain) do not include a muscular fatigue-controlling effect, which is recited in applicants' claims.

Applicants' claims do not recite folate which is required by Hageman et al.

The method disclosed in Harris et al. is directed to administering beta-alanine along with L-histidine and/or creatine, orally or by injection, to increase the content of beta-alanine alone or to increase the content of beta-alanine with L-histidine and/or creatine in blood plasma, thereby increasing the synthesis of beta-alanylhistidine dipeptide and creatine. Namely, Harris et al. disclose increasing the anaerobic working capacity of muscles and other tissues by increasing the beta-alanylhistidine content in blood plasma.

On page 4 of the May 4, 2004 Office Action, the following is stated:

"Harris teaches administration of chicken broth, which contains anserine and carnosine, to subjects (example 2). Harris et al. teaches the additional use of creatine and carbohydrates, such as sugar, in the composition (claims)."

However, chicken broth contains not only anserine and carnosine, but creatine, collagen, amino acid and vegetables for flavor. The May 4, 2004 Office Action does not state that there is a sufficient amount of anserine in chicken broth to provide a muscular fatigue-controlling effect. Although Harris et al. disclose simple carbohydrates, "ribose" is not specifically mentioned. Accordingly, there are many possible combinations of various sugars and various components in chicken broth. It is respectfully submitted that one having ordinary skill in the art could not predict with any degree of certainty that out of the many combinations encompassed by Harris et al., that applicants' combination of anserine and D-ribose would provide a synergistic effect.

Reconsideration is requested for the DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA dated February 16, 2004, which serves to supplement the September 30, 2002 MATAHIRA DECLARATION.

The February 16, 2004 MATAHIRA DECLARATION provides a statistical evaluation of the data obtained from ten mice in each group, which verifies the synergistic results exhibited in a simultaneous administration of anserine and D-ribose.

As seen in Fig. 1 of the February 16, 2004 DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA, an annotation for P-values on the top of bars 4, 5 and 8 in the graph has been included, which makes it clear that there is a statistical significance in the difference between the pair of groups of interest, namely bar 4 vs. bar 8 and bar 5 vs. bar 8. By taking account of this, it is respectfully submitted that one of ordinary skill in the art would undoubtedly conclude that the simultaneous administration of anserine and D-ribose according to the presently claimed invention is unexpectedly superiorly effective to enable mice to swim for a prolonged period of time.

In addition to the above, since the simultaneous administration of anserine and D-ribose is carried out with a dosage of 100 mg/kg of body weight for each substance, by comparing this to a dosage of 200 mg/kg of body weight applied in the case of either anserine or D-ribose, one of ordinary skill in the art would readily conclude that the superiority of such

simultaneous administration of anserine and D-ribose according to the presently claimed invention is not explained by an additive effect resulting from increasing the dosage.

Applicants' presently claimed invention represents the utilization of selected active ingredients, namely anserine and D-ribose, which are potentiated in a synergistically effective manner for attaining superior anti-fatigue activity when administered simultaneously.

It is respectfully submitted that one of ordinary skill in the art could not have been expected to achieve synergistic results with respect of anti-fatigue activity of selected substances (in this case anserine and D-ribose), unless there was a suggestion in the prior art. Both Harris et al. and St. Cyr et al. do not provide such a suggestion.

St. Cyr et al. describe that by administering a pentose, ATP synthesis is accelerated, and the energy useful for mammals can be increased. By the administration of only ribose, the synthesis of ATP can be accelerated, but the consumption rate of ATP cannot be improved. In this regard, in Test Example 2 of the June 25, 2003 MATAHIRA DECLARATION, it was shown that anserine activates

the ATPase in muscles and increases the consumption rate of ATP as the energy source.

It is respectfully submitted that one of ordinary skill in the art would not have considered to combine such references. However, for the reasons discussed below, even assuming *arguendo* that such references are combinable, combining the teachings of Harris et al. and St. Cyr et al. would not result in the presently claimed invention.

The phenomenon of the present invention relies upon a totally new and unexpected discovery in the field. Namely, when anserine and D-ribose are used in combination, not only is ATP synthesis accelerated by ribose, but also the consumption rate of ATP is accelerated by anserine and, as a result, energy can be remarkably increased. None of the fundamental mechanisms for anti-fatigue activities of imidazole related compounds have been shown to be related to that of D-ribose. The present invention provides a method and composition to utilize these effects and/or activities derived from anserine and D-ribose in a synergistic way, not in an antagonistic way, to achieve superior anti-fatigue activities.

It is therefore respectfully submitted that the applicants' claimed invention is not rendered obvious over the references, either taken singly or combined in the manner relied upon in the Office Action, in view of the many distinctions discussed hereinabove. It is moreover submitted that there are no teachings in the references to combine them in such a manner relied upon in the Office Action.

Reconsideration is requested. Allowance is solicited.

Enclosed is a check for \$104 in payment of one additional total claim and one additional independent claim.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



RICHARD S. BARTH
REG. NO. 28,180

FRISHAUF, HOLTZ, GOODMAN & CHICK, P.C.
767 THIRD AVENUE - 25TH FLOOR
NEW YORK, NEW YORK 10017-2023
Tel. Nos. (212) 319-4900
(212) 319-4551/Ext. 219
Fax No. (212) 319-5101
E-Mail Address: BARTH@FHGC-LAW.COM
RSB/ddf

Enc.: Check for \$104